bioavailability of a test formulation of 10 mL of lisinopril oral solution, 1 mg/M1 (formulation F-7), to an equivalent oral dose of the commercially available comparator product, Zestril® lisinopril 10 mg tablet, when administered under fasted conditions in healthy adults.

Study design: Fifty-six healthy adult subjects received a single 10 mL dose of lisinopril oral solution, 1 mg/mL, formulation F-7 (Treatment A), in one period and a separate single dose of Zestril 10 mg tablet (Treatment B) in another period. Screening assessments were performed by the investigator or designee within 28 days prior to study start. Each treatment was administered after an overnight fast of at least 10 hours. Treatment A was administered via a 10 mL oral dosing syringe and followed with 240 mL of room temperature tap water. Treatment B was administered with 240 mL of room temperature tap water. The subjects fasted for 4 hours after dosing. Except for the 240 mL of room temperature water provided with the dose, no water was consumed for 1 hour prior through 1 hour postdose. Each drug administration was separated by a washout period of at least 7 days.

During each study period, meals were the same and scheduled at approximately the same times relative to dose. In addition, during each period, blood samples were obtained prior to and following each dose at selected times through 96 hours postdose. Pharmacokinetic samples were analyzed for lisinopril using a validated analytical method; appropriate pharmacokinetic parameters were calculated for each formulation using non-compartmental methods. Blood was also drawn and urine collected for clinical laboratory testing at screening and at the end of the study.

Statistical Methods: The concentration-time data were analyzed using noncompartmental methods in Phoenix™ WinNonlin® (Version 6.3, Pharsight Corporation). Concentration-time data that were below the limit of quantitation (BLQ) were treated as zero in the data summarization and descriptive statistics. In the pharmacokinetic analysis, BLQ concentrations were treated as zero from time-zero up to the time at which the first quantifiable concentration was observed; embedded and/or terminal BLQ concentrations were treated as "missing". Actual sample times were used for all pharmacokinetic and statistical analyses. Analysis of variance (ANOVA) and the Schuirmann's two one-sided t-test procedures at the 5% significance level were applied to the log-transformed pharmacokinetic exposure parameters, C_{max}, AUC_{last}, and AUC_{inf}. The 90% confidence interval for the ratio of the geometric means (Test/Reference) was calculated. Bioequivalence was declared if the lower and upper confidence intervals of the log-transformed parameters were within 80% to 125%.

Results: Based on the geometric mean ratios of lisinopril AUCs (Test/Reference for AUC_{last} and AUC_{inf}), the bioavailability of the test formulation relative to the reference product was approximately 94% to 95%. The geometric mean ratio of lisinopril C_{max} was 94.11%. The 90% confidence intervals about the geometric mean ratios (Test/Reference) of lisinopril C_{max} and AUCs were within the accepted 80% to 125% range, indicating no significant difference.

Example J

Clinical Trial: Bioavailability Study of 10 mg Lisinopril Oral Solution Vs. Zestril® 10 mg Tablets Under Fed Conditions

This study was conduct the same as in example G, with the exceptions that only 52 subjects were analyzed for pharmacokinetic parameters, and the dose administration followed a 10-hour overnight fast, followed by the ingestion of a Food and Drug Administration standard high-calorie, high-fat breakfast meal.

Results: Based on the geometric mean ratios of lisinopril AUCs (Test/Reference for AUC_{last} and AUC_{inf}), the bioavailability of the test formulation relative to the reference product was approximately 99% to 101%. The geometric mean ratio of lisinopril C_{max} was 99.45%. The 90% confidence intervals about the geometric mean ratios (Test/Reference) of lisinopril C_{max} and AUCs were within the accepted 80% to 125% range, indicating no significant difference.

While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

What is claimed is:

1. A stable oral liquid formulation, comprising:
(i) about 1 mg/ml lisinopril or a pharmaceutically acceptable salt or solvate thereof;
(ii) about 150 mg/ml of a sweetener that is xylitol;
(iii) a buffer comprising about 0.86 mg/ml citric acid and about 1.44 mg/ml sodium citrate;
(iv) about 0.8 mg/ml of a preservative that is sodium benzoate; and
(v) water;
wherein the pH of the formulation is between about 4 and about 5; and
wherein the formulation is stable at about 25±5° C. for at least 12 months.

2. The formulation of claim **1**, wherein the lisinopril is lisinopril dihydrate.

3. The formulation of claim **1**, wherein the pH is about 4.9.

4. The formulation of claim **1**, wherein the formulation is stable at about 25±5° C. for at least 18 months.

5. The formulation of claim **1**, wherein the formulation is stable at about 25±5° C. for at least 24 months.

6. A stable oral liquid formulation, comprising:
(i) about 0.7% (w/w of solids) lisinopril or a pharmaceutically acceptable salt or solvate thereof;
(ii) about 97.3% (w/w of solids) of a sweetener that is xylitol;
(iii) a buffer comprising about 0.01 molar citrate;
(iv) about 0.52% (w/w of solids) of a preservative that is sodium benzoate; and
(v) water;
wherein the pH of the formulation is between about 4 and about 5; and
wherein the formulation is stable at about 25±5° C. for at least 12 months.

7. The formulation of claim **6**, wherein the lisinopril is lisinopril dihydrate.

8. The formulation of claim **6**, wherein the buffer comprises citric acid and sodium citrate.

9. The formulation of claim **6**, wherein the pH is about 4.9.